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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/601,267	Applicant(s) WILLIAM, NICOL K.
	Examiner Cynthia B Wilder	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 9, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above, claim(s) *11-17 and 19-25* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-10, 18, 26, and 27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-10, 17, 18, 26 and 27 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that a search of Group I would overlap with a search of the remaining groups, such that it would be more efficient for the USPTO to examine these claims together in a single application than divided among different application.

This is not found persuasive because the different groups have different objectives, different starting materials, different method steps, and different functions. The different inventions are capable of separate use from each and are distinct in that each group is functionally unrelated to each other group. For example the isolated promoter sequence of Group I is functionally unrelated to the method of culturing cells of group II or the method of screening for substances that modulate telomerase activity of Group III or the delivery system for neoplasia control of Group IV or the method of treatment of group V and visa versa. Additionally, the searches of the different inventions are not co-extensive because methods of isolating promoter sequences are not necessarily required for methods of culturing cells or methods of screening for substances that modulate activity or delivery systems or treatment methods and visa versa. The different inventions have divergent subject matters that require different fields of search. Accordingly, the requirement is still deemed proper and is therefore made FINAL.

2. It is noted that a further review of the claims indicate that claim 17 which is drawn to a vector for use in gene therapy should be included in the non-elected Group IV drawn to a delivery system

for neoplasia control. To further prosecution, a telephone call was made to Kenneth Sibley on January 21, 2002 to restrict claim 17 from the elected Group I as being drawn to a non-elected invention. Mr Sibley agreed to withdraw claim 17 from the elected Group I without traverse. Accordingly, claims 1-10, 18, 26 and 27 are pending in the instant application. Claim 11-17, and 19-25 are withdrawn from further consideration as being drawn to a non-elected invention.

Priority

3. Acknowledgment is made of Applicant's claim for foreign priority based on an application filed in United Kingdom on 1/29/1998. It is noted, however, that Applicant has not filed a certified copy of the 9801902.9 application as required by 35 U.S.C. 119(b). Accordingly, foreign priority based on application 9801902.9 filed on 1/29/1998 has not been granted.

Abstract

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 35. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The disclosure is objected to because the specification at page 5 (last paragraph) and page 45, line 11 indicate that the hProm505 construct is position at -463 as shown in Figure 4a. A review of Figure 4a indicates that the hProm505 construct is position at -436.

Appropriate correction is required.

Claim Objections

7. Claims 26 and 27 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 26 is drawn to a nucleic acid construct comprising an isolated promoter sequence according to claim 6 whereas claim 6 is drawn to a nucleic acid construct comprising a promoter sequence according to claim 1, operably linked to a heterologous gene. Claims 26 does not further limit claim 6 from which it depends because claim 26 only repeats every limitation of claim 6. The same explanation applies for claim 27 which does not further limit claim 8 from which it depends but rather only repeat the limitations of claim 8.

Claim Rejections - 35 USC § 101/112: "Use" Claim

8. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claim 18 provides for the use of a vector in the preparation of a medicament for the treatment of cancer, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process Applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 18 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex*

parte Dunki, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112: Lack of Enablement

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 1, 4-10, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "an isolated promoter sequence having approximately 505 bp upstream of the transcription start site of a human telomerase RNA gene sequence as shown in SEQ ID NO: 36 and wherein said isolated promoter sequence initiates transcription of DNA operably linked downstream of said promoter", it does not reasonably provide enablement for "an isolated promoter sequence derived from the telomerase RNA (TR) gene promoter, having approximately 505 bp upstream of the transcription start site or fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The first paragraph of section 112 requires the specification describe how to make or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation

is undue (*See In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factor include, but are not limited to:

I. Quality of Experimentation Necessary:

The claimed invention is drawn to an isolated promoter sequence derived from the telomerase RNA (TR) gene promoter, having approximately 505 bp upstream of the transcription start site or fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter. At page 3 of the specification, Applicant cites US Patent 5,583,016 as disclosing that the mammalian telomerase RNA gene is a 2.4 kb sequence. Beginning at page 5 of the specification, Applicant discloses that the human telomerase promoter sequence of the instant invention comprises a sequences of the nucleotides as shown in Figure 4a and may further comprise one or more fragments thereof for the sequence as shown in Figure 4a sufficient to promote gene expression. Applicant further describes at page 26, that Figure 1 shows the 1764 bp genomic nucleotide sequence of the human telomerase gene encompassing the gene promoter. Applicant discloses that Figure 4a (SEQ ID NO: 36) is the nucleotide sequence (867 bp) of the human telomerase RNA gene 5' flanking region and Figure 5 shows the detection of promoter activity in the 5' flanking region of the human telomerase RNA gene.

Although Applicant discloses the genomic nucleotide sequence of the human telomerase RNA gene comprising the promoter gene sequence as known in the prior art (Villeponteau, US 5,583,016 and US 6,054,575), the specification fails to adequately describe the isolated promoter sequence derived from the telomerase RNA gene promoter and fragments thereof as claimed, i.e., a nucleotide sequence which includes any regulatory sequences in the 5'-region of the gene and RNA

component coding region. The specification does not discloses any length limitation of the claimed isolated promoter nor does the specification describe or disclose the various substitutions, insertions or deletions, that are encompassed by the fragments thereof of the claimed sequence or the large number of undisclosed mutations. e.g., truncations, nonsense mutations, etc. encompassed by the claims. Still further, specification does not provide any information to enable one of ordinary skill in the art to make or use the claim isolated promoter sequence comprising any mutant, allele, derivatives or variant thereof of the promoter sequence as claimed. In the Detailed Description and Examples beginning at page 32, the specification identifies four constructs of the human telomerase gene promoter which exhibits promoter activity when fused to a firefly luciferase reporter gene, including the construct hProm505 which exhibits the highest promoter activity (see pages 44 and 45 and Fig 4a and 5a). The specification however provides no information to enable one or ordinary skill in the art to isolate a promoter sequence and/or fragments thereof comprising any conceivable sequence derived from the telomerase gene or any conceivable alteration in those sequences besides those four constructs previously mentioned. As to the quality of experimentation required, one of skill in the art would have to design an experimental procedure to isolate a promoter sequence derived from the telomerase RNA gene and fragments thereof that is commensurate with the entire scope of the claims.

II. Amount of Direction and Guidance:

The specification does not provide an isolated promoter derived from a telomerase RNA gene promoter, having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter that bears

a reasonable correlation to the entire scope of the claims. The Detail Description and Examples beginning at page 32 of the specification lack information concerning how to isolate any promoter sequence derived from the telomerase RNA or fragments thereof. The specification further does not disclose or describe any of the numerous modifications encompassed by the isolated promoter of claims as written. Therefore, it would be impossible to predict with certainty the effects of the numerous insertions, deletions, frameshift and nonsense mutations on the functionally of the isolated sequence. In order to make an accurate assessment of the modifications encompassed by the claimed invention would require undue experimentation.

III. Presence and Absence of Working Examples:

The specification of the claimed invention lacks proper working examples. Beginning at page 34, the specification teaches cloning of sequences encompassing the human and mouse telomerase RNA genes. At pages 35 and 36, the specification teaches construction of luciferase reporter gene constructs to determine promoter activity. At page 37, the specification teaches tumor specific regulation of telomerase RNA gene expression visualized by *in situ* hybridization. At page 44 and 45, the specification teaches transfection assays to detect promoter activity in the 5' flanking regions of the human and mouse telomerase RNA genes and at pages 46-48, the specification discloses the identification of key sequence elements involved in transcription factor binding. Nowhere in the Detailed Description pages or Examples does the specification disclose isolation of a promoter sequence derived from the telomerase RNA gene or fragments thereof as claimed in the instant invention. Nowhere in the Detailed Description or Examples does the specification disclose the numerous modifications and mutations encompassed in the isolated sequences as claimed.

Merely making reference to an isolated promoter sequence derived from the telomerase RNA gene promoter, having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter as being encompass in the invention does not enable the practitioner to reproduce the results as reported in the specification for the broad scope of the claimed invention. Thus undue experimentation is required.

IV. Nature of the Invention:

The nature of the invention is an isolated promoter sequence derived from the telomerase RNA gene promoter having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA linked downstream of said promoter. The full scope of the claimed invention is not reproducible due to the lack of guidance presented in the Detailed Description and Examples beginning at page 32. As noted, the specification does not properly disclose an isolated promoter sequence derived from the telomerase RNA gene promoter, having approximately 505 bp upstream of the transcription start site or a fragment thereof that bears a reasonable correlation to the entire scope of the claims.

V. Level of Predictability and Unpredictability in the art:

The specification has not enable an isolated promoter sequence derived from the telomerase RNA gene promoter, having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter commensurate in scope with the claims. Given the large size of the telomerase RNA gene (2.5 kb) or the RNA component of the telomerase RNA gene comprising promoter elements(1.5 kb)

as taught by Villeponteau et al. (US 5,583,016, col. 8-11 and SEQ ID NO: 3 and US 6,054,575, col. 8-11 and SEQ ID NO: 3), it would be unpredictable that any sequence or fragment thereof derived from the telomerase gene or RNA component of the gene is capable of initiating transcription. Likewise, while techniques of mutagenesis are known, it is not routine in the art to screen for multitudes of insertions, deletions, substitutions, and nonsense mutations as encompassed by the instant claims. Additionally, the results of any modification is unpredictable since a reasonable expectation of success is limited by a lack of knowledged concerning the functionality of all the possible mutations on promoter activity or telomerase RNA expression. Therefore, without sufficient knowledged and guidance, isolating a promoter sequence derived from the telomerase RNA gene, having approximately 505 bp upstream of the transcription start site or fragments thereof is unpredictable and the experimentation left to those in the art is unnecessarily and improperly extensive and undue.

For all of the foregoing reasons, undue experimentation is necessary for one of skill in the art to obtain the claimed invention.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 1, 4-10, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. The claimed invention is drawn to an isolated promoter sequence derived from the telomerase RNA (TR) gene promoter, having approximately 505 bp upstream of the transcription start site or fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter. At page 3 of the specification, Applicant cites US Patent 5,583,016 as disclosing that the mammalian telomerase RNA gene is a 2.4 kb sequence. Beginning at page 5 of the specification, Applicant discloses that the human telomerase promoter sequence of the instant invention comprises a sequences of the nucleotides as shown in Figure 4a and may further comprise one or more fragments thereof for the sequence as shown in Figure 4a sufficient to promote gene expression. Applicant further describes at page 26, that Figure 1 shows the 1764 bp genomic nucleotide sequence of the human telomerase gene encompassing the gene promoter. Applicant discloses that Figure 4a (SEQ ID NO: 36) is the nucleotide sequence (867 bp) of the human telomerase RNA gene 5' flanking region and Figure 5 shows the detection of promoter activity in the 5' flanking region of the human telomerase RNA gene.

Although Applicant discloses the genomic nucleotide sequence of the human telomerase RNA gene comprising the promoter gene sequence as known in the prior art (Villeponteau, US 5,583,016 and US 6,054,575), the specification fails to adequately describe the isolated promoter sequence derived from the telomerase RNA gene promoter and fragments thereof as claimed, i.e., a nucleotide sequence which includes any regulatory sequences in the 5'-region of the gene and RNA component coding region. The specification does not discloses the various substitutions, insertions or deletions, that are encompassed by the fragments thereof of the claimed sequence or the large number of undisclosed mutations. e.g., truncations, encompassed by the claim. Still further,

specification does not provide any information on any mutant, allele, derivatives or variant thereof of the promoter sequence as claimed which also encompasses a large genus of nucleic acid sequences not adequately described or disclosed. The claimed "isolated promoter sequence derived from the telomerase RNA gene promoter, having approximately 505 bp upstream, of the transcription start site or fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter" is described in the specification by a limited number of constructs of SEQ ID NO: 36 as depicted in Figure 4a. Each of the claimed inventions is a genus for which a representative number of species of each genus must be disclosed to meet the written description requirement of 112, first paragraph. The specification however provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "Applicant must convey with reasonable clarity to those in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*". (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invent what is claimed" (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acid sequences, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd,* 18 USPQ2d 1016. In *Fiddes v. Baird,* 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co.,43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an Applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, the nucleic acid sequences encompassed by the claims do not meet the written description provision of 35 USC 112, first paragraph. The species disclosed herein is not a representative of the genus because the genus is highly variant. Accordingly, the specification fails

to show that Applicant was, in fact "in possession of the claimed invention" at the time the application for patent was filed. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is separable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 112: Indefiniteness

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

14. Claims 1-10, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 1-10, 26, 27 are indefinite in claim 1 for the recitation of "derived from" because it is unclear how many modifications are encompassed by "derived from". Additionally, the actual sequence composition of the claimed isolated promoter and the relationship of the isolated promoter sequence to the"telomerase RNA gene promoter" cannot be clearly ascertained. Clarification is required as to the actual sequence composition of the "isolated promoter sequence".

(b) Claims 1-10, 26 and 27 are indefinite in claim 1 for the recitation of "fragment thereof" because the definition in the specification at page 5 is ambiguous and it cannot be determined from the specification or claims whether the "fragments thereof" are related to fragments of the claimed isolated promoter sequence or fragments of the telomerase gene. Clarification is required as to the actual sequence composition of the "isolated promoter sequence" and functional fragments thereof if present".

(c) Claims 1-10, 26 and 27 are indefinite in claim 1 for the recitation of "capable of" because it cannot be determined whether the limitations after "capable of " is property of the isolated promoter sequence or the telomerase gene or fragments thereof or a separate entity. It is suggested amending the claim 1 to recite active, positive language by changing "capable of initiating" to "which initiates" or some other language as supported by the specification as originally filed.

(d) Claim 1 lacks proper antecedent basis for "the transcription start site" because no prior reference has been made to a "transcription start site" nor has any structural sequence been identified.

(e) Claims 2 and 3 are indefinite for the recitation of "as shown in Fig 4a and Fig 5a" because Figure 4a and 5a depict several different constructs of the telomerase RNA gene promoter including hProm505 but does not identify only hProm505 encompassing SEQ ID NO: 36. Likewise, Fig. 5a depicts a bar graph and does not relate to a sequence. Thus it cannot accurately be determined the relationship between the figures 4a and 5a and SEQ ID NO: 36.

(f) Claims 4 is indefinite at the recitation of "mutant, allele, derivative or variant thereof" because the definition at pages 8 and 9 is ambiguous. Thus it cannot be determined the relationship of the "mutant, allele, derivative or variants thereof" in regards to the claimed isolated promoter sequence. More specifically it cannot be determined from the information given what sequences or modification thereof derived from the telomerase RNA gene promoter are encompassed by the recitation of "mutant, allele, derivative or variants thereof". Clarification is required as to Applicant's intent.

Claim Rejections - 35 USC § 102(b)

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 4-6, 8-10, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Villeponteau et al. (*US 5,583,016, December 10, 1996*). Applicant has claimed an isolated promoter sequence derived from the telomerase RNA (TR) gene promoter, having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter.

Villeponteau et al. disclose an isolated promoter sequence derived from the telomerase RNA gene promoter having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter (See columns 8-11, SEQ ID NO: 3, col. 18, lines 66-67 to col. 19, lines 1-21. See also columns 47-51, claims 10-21.). Therefore, the claim 1 as broadly written is anticipated by the reference of Villeponteau et al.

Regarding claim 4, Applicant broadly defines allele, mutant, variant or derivative by way of nucleotide addition, substitution or deletion of a promoter sequence (see page 8). Thus Villeponteau et al. encompass the claimed invention. Villeponteau et al. teach an isolated promoter sequence according to claim 1 having a derivative or allele or variant thereof of the sequence as shown in Fig 4a (SEQ ID NO: 36) [(see SEQ ID NO: 3, col. 8-11)].

Regarding claim 5, Applicant defines "heterologous nucleic acid coding sequence" as a coding sequence form another source other than from the telomerase RNA gene, e.g., reporter gene (page 11). Thus Villeponteau et al. encompass the claim invention. Villeponteau et al. disclose an isolated prompter sequence according to claim 1 operably linked to a heterologous nucleic acid coding sequence (col. 19, lines 7-21).

Regarding claim 6 and 26, Villeponteau et al. disclose a nucleic acid construct comprising a promoter sequence according to claim 1, operably linked to a heterologous gene (see col. 8, lines 5-26, col. 19, lines 16-30 and Example 7).

Regarding claim 8 and 27, Villeponteau et al. disclose a vector comprising an isolated promoter sequence according to claim 1(see col. 8, lines 9-15 and Example 7).

Regarding claim 9, Villeponteau et al. disclose a host cell comprising an isolated promoter sequence according to claim 1 (col. 3, lines 45-47 and col. 4, lines 1-8 and Example 7).

Regarding claim 10, Villeponteau et al. disclose a host cell comprising a nucleic acid construct according to claim 6 (col. 3, lines 45-47 and col. 4, lines 1-8, and Example 7). In view of the foregoing, the claims 4-6, 8-10, 26 and 27 as broadly written are anticipated by the reference of Villeponteau et al.

Claim Rejections - 35 USC § 102(a)

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the Applicant for a patent.

18. Claims 1-6, 8-10, 26 and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Zhao et al. (Oncogene, Vol. 16, pages 1345-1350, March 1998). Regarding claim 1, Zhao et al. teach an isolated promoter sequence derived from the telomerase RNA (TR) gene promoter, having approximately 505 bp upstream of the transcription start site or a fragment thereof, capable of initiating transcription of DNA operably linked downstream of said promoter (see page 1347, figure 2). Therefore, Zhao et al. meets all of the claim limitation of claim 1.

Regarding claim 2, Zhao et al. teach an isolated promoter sequence according to claim 1 wherein the promoter sequence is construct hPRom505 as shown in Fig 4a (See page 1347, Figure 2 and column 1, first full paragraph).

Regarding claim 3, Zhao et al. teach an isolated promoter sequence according to claim 1 wherein the promoter sequence is 230 bp in length starting at position -42 bp as shown in Fig 4a (see page 1347, Figure 2 and col. 1, first full paragraph).

Regarding claim 4, Zhao et al. teach an isolated promoter sequence according to claim 1 having the sequence as shown in Fig 4a (see page 1347, Figure 2).

Regarding claim 5, Zhao et al. teach an isolated promoter sequence according to claim 1 operably linked to a gene (page 1349, beginning at the 9^{th}-11^{th} line from bottom of column 2)

Regarding claims 6 and 26, Zhao et al. teach a nucleic acid construct comprising a promoter sequence according to claim 1, operably linked to a heterologous gene (see page 1347, Figure 2 and page 1349, col. 2, first full paragraphs and the 9^{th}-11^{th} line from bottom of column 2).

Regarding claims 8 and 27, Zhao et al. teach a vector comprising an isolated promoter sequence according to claim 1 (see page 1349, "Materials and Methods", last paragraph of col. 1 bridging col. 2).

Regarding claim 9, Zhao et al. teach host cell comprising an isolated promoter sequence according to claim 1 (see page 1349, "Materials and Methods", last paragraph of col. 1 bridging col. 2).

Regarding claim 10, Zhao et al. teach a host cell comprising a nucleic acid construct according to claim 6 (see page 1349, last full paragraph of column 2). Therefore, the reference of Zhao et al. also meets all of the limitations of claims 2-6, 8-10, 26, and 27.

Prior Art

17. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Feng et al. (Science, Vol. 269, pages 1236-1241, September 1995) teach the RNA component of the human telomerase gene which encompasses telomerase RNA promoter elements (see Figure 2, page 1237). Hickley et al. (Nucleic acids Research, Vol. 26, No. 2, pages 532-536, January 15, 1998) teach the identification of the mouse and human telomerase RNA template sequence and also the 5' end of the human telomerase RNA 45 nucleotide from the telomerase RNA template sequence. The reference identifies fragments of the telomerase RNA promoter elements in specified regions (page 534, right column). The references cited above are not relied upon because they encompass similar teachings as recited in the prior art of the rejections.

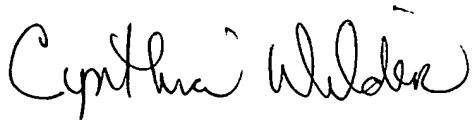
Conclusion

17. No claims are allowed. However, claim 7 is free of the prior art because the prior art does not teach or suggest a nucleic acid construct comprising a sequence of the telomerase RNA gene operably linked to a heterologous gene which encodes a cytotoxin. No motivation was found in the prior art to operably link a sequence from the telomerase RNA gene to a gene which encodes a cytotoxin. Accordingly an obviousness-type rejection could not be made against the claim.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Group's receptionist at (703) 308-0196.



cbw
February 10, 2003

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